October 6, 2000

Ronald L. Joiner, Ph.D.
Manager, Global Toxicology
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201

Dear Dr. Joiner:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plans for Cyclic neopentanetetrayl diphenyl ester of phosphorous acid (CAS # 144-35-4) and p-Cumylphenol (CAS # 599-64-4), submitted May 25, 2000. I commend GE Plastics for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program Web site EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the Chemical RTK Web site within the next few days.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
N. Patel
A. Abramson

EPA Comments on Chemical RTK Challenge Submission:

p-Cumylphenol

SUMMARY OF EPA COMMENTS

The sponsor, GE Plastics, submitted Robust Summary information dated May 31, 2000 to EPA and a test plan to the industry HPV Tracking System Web site (www.hpvchallenge.com). EPA posted the cover letter and robust summary submission on the ChemRTK Web site on June 13, 2000. The proposed information-gathering plan is for p-Cumylphenol (p-(á, á-dimethylbenzyl)phenol, CAS # 599-64-4).

EPA has reviewed this submission and has reached the following conclusions:

1. The submission comprised a minimally acceptable test plan overall.

2. Chemical characterization. A brief statement of the uses of the chemical would help reviewers assess the appropriateness of some of the proposed tests.

3. Proposed health endpoint testing: Acute toxicity. EPA questions the proposal to conduct more acute toxicity studies. There is no rationale presented for the proposal, and the sponsor has submitted an adequate summary of an acute oral study.

4. Proposed health endpoint testing: Developmental toxicity. The proposal includes conducting a combined repeat dose/reproductive/developmental toxicity screening test (OECD Test Guideline 422) in addition to a pre-natal developmental toxicity test (OECD 414). There is no rationale presented for conducting both tests. The OECD 422 screening study is sufficient to cover all three endpoints (repeat dose, reproductive and developmental toxicity) for the purposes of the U.S. HPV Challenge Program.

5. Proposed health endpoint testing: Genotoxicity. EPA notes a discrepancy between the test plan summary sent to the EPA and posted on the EPA Web site and the test plan posted on the industry HPV Tracking System at www.hpvchallenge.com. The latter proposes to conduct another *Salmonella* assay on the HPV chemical whereas the former does not. The robust summary submitted for this endpoint is adequate for the purposes of the U.S. HPV Challenge Program and there is no need to repeat the study.

5. Proposed health and ecological effects testing: The sponsor proposes to perform testing beyond the recommendations of the U.S. HPV Challenge Program. EPA presumes that these tests may be needed for purposes outside of the U.S. HPV Challenge Program. See comments on this issue from the sponsor under “Letter of Clarification” for this submission on this Web site.

6. Fate. The model to be used is not specified. EPA recommends that the EQC Level III model be used to estimate transport and distribution for the purposes of the U.S. HPV Challenge Program.

EPA COMMENTS ON THE p-CUMYLPHENOL CHALLENGE SUBMISSION

General

The sponsor supplied a minimally acceptable package. However, the test plan on the industry HPV Tracking System Web site and the test plan summary table preceding the robust summaries submitted to the EPA did not agree in all respects.

There was no statement about the uses of the HPV chemical, which makes it difficult to assess the appropriateness of some of the proposed tests (e.g., whether there is a need to conduct an acute dermal toxicity test).

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The sponsor's approach for these endpoints should satisfy the needs of the U.S. HPV Challenge Program

Fate (photodegradation, stability in water, biodegradation, and transport/distribution).

EPA believes the sponsor's approach should satisfy these endpoints. However, the test plan does not specify the model to be used for transport/distribution estimation. EPA prefers the EQC Level III fugacity model (available free from http://www.trentu.ca/academic/aminss/envmodel/) for the U.S. HPV Challenge Program.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

EPA believes the sponsor's approach should satisfy these endpoints. However, EPA also notes:

Proposed health endpoint testing: Acute toxicity. EPA questions the proposal to conduct two acute toxicity studies using the inhalation and dermal routes of administration. There is no rationale presented for conducting both studies, especially since an adequate acute oral study has already been performed. (NOTE: There is a discrepancy between the test plan summary sent to EPA and posted on the EPA Web site and the test plan posted on the industry HPV Tracking System at www.hpvchallenge.com. The former proposes to perform inhalation and dermal acute toxicity studies and the latter proposes only to conduct the dermal study).

Proposed health endpoint testing: Genotoxicity. EPA notes another discrepancy between the test plan summary sent to the EPA and posted on the EPA Web site and the test plan posted on the industry HPV Tracking System at www.hpvchallenge.com. The latter proposes to conduct another *Salmonella* assay on the HPV chemical whereas the former does not. EPA's position is that the robust summary submitted for this endpoint is adequate for the purposes of the U.S. HPV Challenge Program and there is no need to repeat the study. In addition, the sponsor is proposing to conduct an *in vivo* genotoxicity study, which is beyond the needs of the U.S. HPV Challenge Program. There is no rationale presented for conducting the *in vivo* genotoxicity test.

Proposed health endpoint testing: Developmental toxicity. The proposal includes conducting a combined repeat dose/reproductive/developmental toxicity screening test (OECD Test Guideline 422) in addition to a pre-natal developmental toxicity test (OECD 414). There is no rationale presented for conducting both tests. The OECD 422 screening study is sufficient to cover all three endpoints (repeat dose, reproductive and developmental toxicity) for the purposes of the U.S. HPV Challenge Program. It is presumed that the OECD 414 study may be needed for some other (regulatory) purposes outside of the U.S. HPV Challenge Program.

Ecological Effects. The proposal includes conducting the acute base set testing on fish (OECD Test Guideline 203), algae (OECD Test Guideline 201), and daphnid (OECD Test Guideline 202). In addition, a daphnid reproduction test (OECD Test Guideline 211) will be conducted. This chronic daphnid test is considered a "conditional" SIDS-level test and may not be necessary for the U.S. HPV Challenge Program. The results of the water solubility, partition coefficient, and acute aquatic toxicity tests will determine the need for such a test.

Specific Comments on Robust Summaries

EPA evaluations are based on the guidance document available at http:\\www.epa.gov/opptintr/chemrtk/guidocs.htm.

EPA evaluated the two health robust summaries and found them both to be adequate for the purposes of the U.S. HPV Challenge Program. (The following comments reflect the information in the robust summaries; information in the full study reports may address the comments):

Acute Toxicity. The following information was missing: (1) the purity of test substance, and (2) the number of animals that died by dose group and day

Genotoxicity Studies. The following information was missing: (1) the number of replicates per concentration or whether the test was repeated; (2) the type of inducer used to prepare the S9 fraction;

and (3) the criteria used to judge whether the chemical was positive or negative.